systems. For instance, Anx-A1 has been shown to exert homeostatic control over cells of the innate immune system such as neutrophils and macrophages, and also to play a role in T-cells by modulating the strength of T-cell receptor (TCR) signalling (D'Acquisto et al., *Blood* 109: 1095-1102, 2007). Use of a neutralising antibody against Anx-A1 to inhibit its roles in the adaptive immune system has been shown to be effective in the treatment of various T-cell-mediated diseases, including autoimmune diseases such as rheumatoid arthritis and multiple sclerosis (WO 2010/064012; WO 2011/154705).

[0012]   Antibodies against Anx-A1 have also been shown to be useful in the treatment of certain psychiatric conditions, in particular anxiety, obsessive-compulsive disorder (OCD) and related diseases (WO 2013/088111), though the mechanism by which this occurs is unknown.

[0013]   WO 2005/027965 demonstrates that Anx-A1 is localised to the surface of apoptotic cells, and that anti-Anx-A1 antibodies can be used to monitor apoptosis. The document teaches that on this basis such antibodies may thus be used to monitor and diagnose cancer. The document also teaches that Anx-A1 expression on the surface of apoptotic cells inhibits an immune response against the cells. On this basis, the document speculates that an antibody that binds Anx-A1 can be used to treat cancer, by blocking the immunosuppressant effect of Anx-A1 on cells that have commenced apoptosis and thus stimulating an immune response against the cancer.

[0014]   Oh et al. (*Nature* 429: 629-635, 2004) teaches that Anx-A1 is expressed on some solid tumours and may be used as a target to direct radioimmunotherapy to those cancers, and demonstrates that such therapy enhances survival in an animal model of disease. US 2015/0086553 suggests that anti-Anx-A1 antibodies can be used in cancer treatment and diagnosis but fails to teach how such treatment might be performed. The binding of an anti-Anx-A1 scFv to the gastric cancer cell line SNU-1 is demonstrated. Wang et al. (*Biochem. BioPhys. Res. Commun.* 314: 565-570, 2004) demonstrates a correlation between Anx-A1 expression and multi-drug resistance in cancer. Thus several diseases have been shown to display an association with Anx-A1 expression, including cancer. However, prior to the present invention it had not been demonstrated that an anti-Anx-A1 antibody, particularly when used without any co-treatment, could be used to treat cancer.

[0015]   Indeed, the present invention demonstrates that efficacy in the treatment of cancer does not extend to all specific binding molecules which bind human Anx-A1. The present invention provides particular specific binding molecules which bind human Anx-A1 and can advantageously be used to treat cancer, particularly cancer which is resistant to chemotherapy drugs and/or breast cancer, colorectal cancer, ovarian cancer, lung cancer and pancreatic cancer. It is unknown why the specific binding molecules of the invention are effective in cancer treatment, while other specific binding molecules that also bind human Anx-A1 are not. Without being bound by theory, it is speculated that the activity of specific binding molecules that bind human Anx-A1 may be dependent on the epitope recognised.

[0016]   A number of monoclonal antibodies that recognise human Anx-A1 are disclosed in WO 2018/146230. The antibodies disclosed in WO 2018/146230 have particularly advantageous properties, in that they are able to bind to human Anx-A1 with very high affinity. It has now been

discovered by the inventors that the antibodies disclosed in WO 2018/146230 are useful in treating cancer, as described further below.

[0017]   Thus in a first aspect the invention provides a specific binding molecule which binds human Anx-A1 for use in the treatment of cancer in a subject, wherein:

[0018]   (i) said specific binding molecule comprises the complementarity-determining regions (CDRs) VLCDR1, VLCDR2, VLCDR3, VHCDR1, VHCDR2 and VHCDR3, each of said CDRs having an amino acid sequence as follows:

[0019]   VLCDR1 has the sequence set forth in SEQ ID NO: 1, 7 or 8;

[0020]   VLCDR2 has the sequence set forth in SEQ ID NO: 2;

[0021]   VLCDR3 has the sequence set forth in SEQ ID NO: 3;

[0022]   VHCDR1 has the sequence set forth in SEQ ID NO: 4;

[0023]   VHCDR2 has the sequence set forth in SEQ ID NO: 5; and

[0024]   VHCDR3 has the sequence set forth in SEQ ID NO: 6; or, for each sequence, an amino acid sequence with at least 85% sequence identity thereto; and/or

[0025]   (ii) said specific binding molecule binds to Anx-A1 at a discontinuous epitope consisting of amino acids 197-206, 220-224 and 227-237 of SEQ ID NO: 17.

[0026]   Similarly, the invention provides a method of treating cancer in a subject, comprising administering to said subject a specific binding molecule as defined above. Also provided is the use of a specific binding molecule as defined above in the manufacture of a medicament for the treatment of cancer in a subject.

[0027]   In a second aspect, the invention provides a kit comprising a specific binding molecule as defined above and a chemotherapeutic agent.

[0028]   In a third aspect, the invention provides a product comprising a specific binding molecule as defined above and a second therapeutic agent for separate, simultaneous or sequential use in the treatment of cancer in a subject.

[0029]   As mentioned above, the invention provides a specific binding molecule which binds human Anx-A1 for use in the treatment of cancer in a subject. A "specific binding molecule" as defined herein is a molecule that binds specifically to a particular molecular partner, in this case human Anx-A1. A molecule that binds specifically to human Anx-A1 is a molecule that binds to human Anx-A1 with a greater affinity than that with which it binds to other molecules, or at least most other molecules. Thus, for example, if a specific binding molecule that binds human Anx-A1 were contacted with a lysate of human cells, the specific binding molecule would bind primarily to Anx-A1. In particular, the specific binding molecule binds to a sequence or configuration present on said human Anx-A1. When the specific binding molecule is an antibody the sequence or configuration is the epitope to which the specific binding molecule binds. The Anx-A1 epitope bound by the specific binding molecules for use according to the invention is described below.

[0030]   The specific binding molecule for use herein does not necessarily bind only to human Anx-A1: the specific binding molecule may cross-react with certain other undefined target molecules, or may display a level of non-specific binding when contacted with a mixture of a large number of